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## CHANGES IN FRONTO-PARIETAL CONNECTIVITY IN SCHIZOPHRENIA

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outcomes) and more flexible, but computationally demanding model-based behavior (i.e., implementing cognitive models). Model-based/model-free decision-making can be investigated using sequential decision tasks and has been shown to be associated with presynaptic striatal dopamine synthesis. During phases of psychotic remission in schizophrenia, dopamine synthesis in the dorsal striatum is reduced. We hypothesized that particularly model-free decision-making is impaired in schizophrenia during psychotic remission and is associated with (i) abnormal dopamine synthesis in dorsal striatum, (ii) aberrant task-activation in dorsal striatum, and (iii) cognitive difficulties in patients (e.g., reduced speed).

**Methods:** 26 patients with chronic schizophrenia, currently in psychotic remission, and 22 healthy controls (matched by age and gender) were enrolled in the study. Model-based/model-free decision-making was evaluated with a two-stage Markov decision task, followed by computational modeling of subjects' learning behavior. Presynaptic dopamine synthesis was assessed by 18F-DOPA positron emission tomography and subsequent graphical Patlak analysis. Task-activation was measured by functional magnetic resonance imaging. Cognitive impairments were quantified by Trail-Making-Test A (among others). Associations between decision-making parameters, dopamine synthesis, task-activation, and cognitive impairments were tested by correlation analyses.

**Results:** Patients with schizophrenia showed selectively impaired model-free decision-making. 18F-DOPA uptake (i.e., presynaptic dopamine synthesis capacity) in the dorsal striatum was decreased in patients. Impaired model-free decision-making in patients correlated with (i) decreased dopamine synthesis in dorsal striatum, (ii) abnormal task-activation in dorsal striatum, and (iii) lower speed in Trail-Making-Test A.

**Discussion:** Results demonstrate an association of reduced dorsal striatal dopamine synthesis and brain activity with impaired model-free decision-making in schizophrenia, which potentially contributes to cognitive difficulties.

#### S147. FUNCTIONAL BRAIN CONNECTIVITY DATA IMPROVE CLINICAL OUTCOME PREDICTION IN YOUTH AT RISK FOR PSYCHOSIS

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**Background:** Improved outcome prediction in individuals at high risk for psychosis may facilitate targeted early intervention. Studies suggest that improved outcome prediction may be achieved through the use of neurocognitive or neuroimaging data, on their own or in addition to clinical data. This study examines whether adding resting-state functional connectivity data to validated clinical predictors of psychosis improve outcome prediction in the prodromal stage.

**Methods:** This study involves 137 adolescents and young adults at Clinical High Risk (CHR) for psychosis from the Shanghai At Risk for Psychosis (SHARP) program. Based on outcome after one-year follow-up, participants were separated into three outcome categories: good outcome (symptom remission, N = 71), intermediate outcome (ongoing CHR symptoms, N = 30), and poor outcome (conversion to psychosis or treatment-refractory, N = 36). Resting-state fMRI data were acquired for each participant and processed using the Conn toolbox, including rigorous

motion correction. Multinomial logistic regression analysis and leave-one-out cross-validation were used to assess the performance of three prediction models: 1) a clinical-only model using validated clinical predictors from the NAPLS-2 psychosis-risk calculator, 2) an fMRI-only model using measures of functional connectome organization and within/between-network connectivity among established resting-state networks, and 3) a combined clinical and fMRI prediction model. Model performance was assessed using the harmonic mean of the positive predictive value and sensitivity for each outcome category. This F1 measure was compared to expected chance-levels using a permutation test with 1,000 sampled permutations in order to evaluate the statistical significance of the model's prediction.

**Results:** The clinical-only prediction model failed to achieve a significant level of outcome prediction ( $F1 = 0.32$ ,  $F1\text{-chance} = 0.26 \pm 0.06$ ,  $p = .154$ ). The fMRI-only model did predict clinical outcome to a significant degree ( $F1 = 0.41$ ,  $F1\text{-chance} = 0.29 \pm 0.06$ ,  $p = .016$ ), but the combined clinical and fMRI prediction model showed the best performance ( $F1 = 0.46$ ,  $F1\text{-chance} = 0.29 \pm 0.06$ ,  $p < .001$ ). On average, positive predictive values (reflecting the probability that an outcome label predicted by the model was correct) were 39% better than chance-level and 32% better than the clinical-only model. Analyzing the contribution of individual predictor variables showed that GAF functional decline, a family history of psychosis, and performance on the Hopkins Verbal Learning Test were the most influential clinical predictors, whereas modular connectome organization, default-mode and fronto-parietal within-network connectivity, and between-network connectivity among language, salience, dorsal attention, cerebellum, and sensorimotor networks were the leading fMRI predictors.

**Discussion:** This study's findings suggest that functional brain abnormalities reflected by alterations in resting-state functional connectivity precede and may drive subsequent changes in clinical functioning. Moreover, the findings show that markers of functional brain connectivity may be useful for improving early identification and clinical decision-making in prodromal psychosis.

#### S148. MULTIMODAL BRAIN ANALYSIS IN PSYCHOSIS RISK – THE OULU BRAIN AND MIND STUDY

Abstract not included.

#### S149. CHANGES IN FRONTO-PARIETAL CONNECTIVITY IN SCHIZOPHRENIA: TMS AND FNIRS STUDY

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**Background:** One of the most prominent deficits in schizophrenia is impairment in executive function. This impairment is associated to aberrant function of the dorso-lateral prefrontal cortex (DLPFC) (Weinberger et al. 1986) and the fronto-parietal network (FPN) (Deserno et al. 2012). The FPN is involved in cognitive control (Seeley et al. 2007, Zanto & Gazzaley 2013). While correlations of activation of DLPFC and inferior parietal lobe (IPL) are well documented, fMRI based techniques cannot determine causal relationships of interactions between brain regions. We used Transcranial magnetic stimulation (TMS), which directly affects the stimulated brain region and connected brain areas (Valchev et al 2015) and therefore can be used to investigate causal interactions between brain regions. TMS stimulation to the DLPFC at 10 Hz may cause either putative increase or decrease of activation in the in the IPL, depending on whether connections are inhibitory or excitatory (Curtin et al 2019). We hypothesised that patients with schizophrenia would have slower reaction in IPL as a consequence of DLPFC stimulation.

**Methods:** Thirteen patients and fourteen healthy controls (HC) underwent transcranial magnetic stimulation (TMS) to the right DLPFC. TMS consisted of 20 trains of impulses at 10 Hz for 3 seconds, and 60 seconds waiting time. Simultaneously, we measured brain activation IPL using functional near infrared spectroscopy (fNIRS). Diagnostic category was confirmed using MINI plus interview. The severity of symptoms was assessed using the positive and negative syndrome scale (PANSS). We estimated levels of Oxygenised haemoglobin (HbO) using NIRSLab software. GLM was applied using both hemodynamic response function (HRF) and its derivative. T-test was used, with FDR correction, to compare time segments of HbO following TMS stimulation.

**Results:** There was no difference in age and gender between the groups. The two groups differed in education ( $t(2,25) = 2.584$ ,  $p = 0.016$ ). GLM revealed decreased levels of HbO in HC in bilateral IPL following the TMS to the DLPFC ( $p_{\text{bonferroni}} = 0.05$ ). However, when patients were compared to HC higher levels of HbO were observed ( $p = 0.05$ ). However, no difference in derivative of HRF was observed. In addition, there was a significant difference in time courses between patients and HC following TMS stimulation. Namely, while there was an immediate decrease in parietal HbO levels in HC, in SZ first an increase, followed by a decrease was observed. This was significant (at a threshold level of  $p\text{FDR} = 0.05$ ) for several time segments and channels in both right and left IPL.

**Discussion:** We observed differences in activation of bilateral IPL as a consequence of DLPFC stimulation in patients with schizophrenia. Namely, there was an initial increase in HbO levels, as opposite to HC who had an immediate decrease in HbO level. This indicates opposite function of information processing from the frontal to parietal lobe in schizophrenia patients. This is in line with the idea of impaired fronto-parietal inhibition in schizophrenia which has been proposed to underlie impairments in schizophrenia such as lack of cognitive control.

## S150. EMOTIONAL BEHAVIOUR IN HIGH-RISK AND FIRST-EPISEDE PSYCHOSIS

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**Background:** Studies indicate that people with schizophrenia and first-episode psychosis experience deficits in their ability to accurately detect and display emotions through facial expressions, and that functioning and symptoms are associated with these deficits. This study aims to examine how emotion recognition and facial emotion expression are related to functioning and symptoms in a sample of individuals at ultra-high risk, first-episode psychosis and healthy controls.

**Methods:** During fMRI, we combined the presentation of emotional faces with the instruction to react with facial movements predetermined and assigned. 18 patients with first-episode psychosis (FEP), 18 individuals at ultra high risk of psychosis (UHR) and 22 healthy controls (HCs) were examined while viewing happy, sad, or neutral faces and were instructed to simultaneously move the corners of their mouths either (a). upwards or (b). downwards, or (c). to refrain from movement. The subjects' facial movements were recorded with an MR-compatible video camera.

**Results:** Neurofunctional and behavioral response to emotional faces were measured. Analyses have only recently commenced and are ongoing. Full results of the clinical and functional impact of behavioral and neuroimaging results will be presented at the meeting.

**Discussion:** Increased knowledge about abnormalities in emotion recognition and behaviour as well as their neural correlates and their impact on clinical measures and functional outcome can inform the development of novel treatment approaches to improve social skills early in the course of schizophrenia and psychotic disorders.

## S151. HIPPOCAMPAL CONNECTIVITY AND VOLUME AS PREDICTORS OF TREATMENT RESPONSE – A REPLICATION STUDY IN TWO PSYCHOSIS COHORTS

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**Background:** Approximately 30% of patients with schizophrenia do not improve with antipsychotic drug (APD) treatment and 60% show sub-optimal response. Converging lines of evidence point to hippocampal dysfunction in schizophrenia. It is thought that hippocampal dysfunction spreads across hippocampal subfields and to cortical regions by way of long-range efferent projections. Our prior studies have shown altered hippocampal regional cerebral blood flow in unmedicated patients and normalization after APD treatment. Meta-analyses show reduced hippocampal volume in first episode psychosis (FEP) patients. We evaluated resting state hippocampal functional connectivity (hFC) as well as hippocampal and hippocampal subfield volumes as predictors of treatment response (TR) in two cohorts of patients with a psychosis spectrum disorder. All patients were subsequently treated with an APD for 6 weeks.

**Methods:** Cohort 1 consisted of 55 medication-naïve first episode psychosis (FEP) subjects (36 male; mean age 24.18 years). Cohort 2 consisted of 42 unmedicated patients with schizophrenia (SZ) (31 male; mean age 27.9 years).

FEP were scanned on a Siemens MAGNETOM Prisma MRI scanner using a 20 channel head coil. Anatomical scans were acquired via T1-weighted and T2-weighted images. Two 6-minute resting state scans were acquired in opposing phase encoding directions (A > P and P > A).

SZ were scanned on a Siemens MAGNETOM Allegra MRI scanner with a circularly polarized transmit/receive head coil. Anatomical scans were acquired via a T1-weighted sequence. Resting state scans were acquired with a single 5-minute gradient recalled echo-planar imaging sequence.

For both datasets, resting state data were preprocessed in the CONN toolbox (version 18a). We used the left hippocampus as a seed region to create whole brain seed-to-voxel correlation maps for each subject. Regression analyses were then performed to assess the relationship between resting state connectivity and TR (% change in BPRS positive score from (A) baseline to (B) after 6 weeks of APD:  $((B-A)/A) \times 100$ ). Analyses were corrected using voxel ( $p < 0.05$ , uncorrected) and cluster level correction ( $p < 0.05$ , FDR corrected). Age, sex, and framewise displacement were used as covariates of no interest.

T1 and T2 weighted images were preprocessed using FreeSurfer 6.0. FreeSurfer's hippocampus subfield segmentation module was used to calculate left and right subfield volumes. SPSS 25 was used to regress hippocampal subfield volumes on TR. Age and estimated total intracranial volume (eTIV) were included as covariates of no interest.

**Results:** In both cohorts greater hFC to the cuneus and precuneus was predictive of better TR, as was greater hFC to the fusiform gyrus, medial prefrontal cortex (PFC) and anterior cingulate cortex in cohort 2. Reduced hFC connectivity to the angular gyrus in supramarginal gyrus and temporal pole in cohort 1 as well as the orbitofrontal cortex and dorsolateral PFC in cohort 2 were also predictive of better TR. Results from the stepwise regression showed that neither right nor left whole hippocampal volume, or subfield volumes, significantly predict TR for either cohort.

**Discussion:** In two patient cohorts, we observed a similar pattern where increased hFC to the cuneus and precuneus was predictive of better response to APD. Furthermore, the lack of a significant predictive value of hippocampal volumes in predicting TR was replicated in each cohort. The replicability of these findings, particularly in a cohort of medication-naïve FEP provides potential biological patterns useful in determining initial response to APD medication in patients with a psychosis spectrum disorder.